Catalyst-Free Deaminative Functionalizations of Primary Amines via Photoinduced Single-Electron Transfer

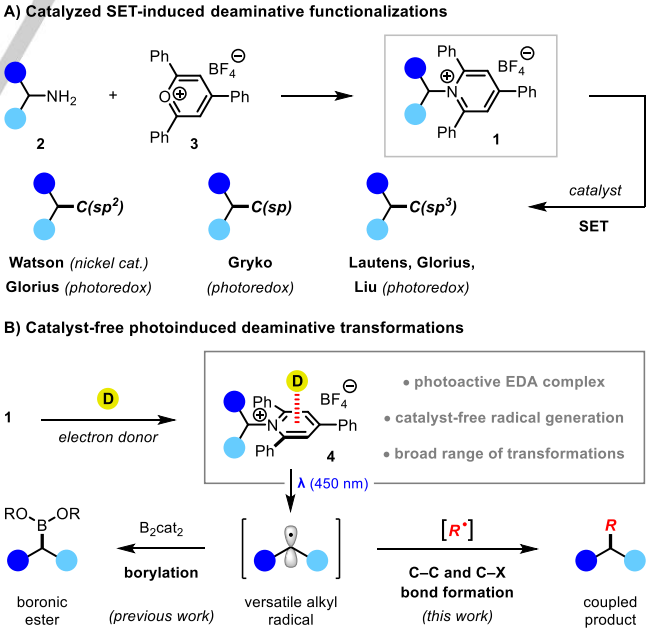
Jingjing Wu,[†] Phillip S. Grant,[†] Xiabing Li, Adam Noble, and Varinder K. Aggarwal*[a]

Abstract: The use of pyridinium-activated primary amines as photoactive functional groups for deaminative generation of alkyl radicals under catalyst-free conditions is described. By taking advantage of the visible-light absorptivity of electron donor–acceptor complexes between Katritzky pyridinium salts and either Hantzsch ester or Et_3N, photoinduced single-electron transfer could be initiated in the absence of a photocatalyst. This general reactivity platform has been applied to deaminative alkylations (Giese), allylations, vinylations, alkynylations, and thioetherifications. The mild conditions are amenable to a diverse range of primary and secondary alkyl pyridiniums and demonstrate broad functional group tolerance.

Visible-light photochemistry in organic synthesis has witnessed a resurgence in research activity over the last decade.[1] This is largely due to a growing appreciation of the synthetic utility of photoredox catalysts, which, upon photoexcitation, function as single-electron or energy transfer catalysts to provide access to free-radical intermediates.[2] An alternative strategy, that circumvents the need for catalysis, is direct photoexcitation of a substrate, which has classically been performed using UV-light.[3] However, recent developments have taken advantage of the visible-light absorptivity of specific functional groups that act as photoactive handles to enable photoinduced electron transfer (PET).[4] Although direct photoexcitation is possible with a number of different functional groups,[5] such reactions more commonly take advantage of electron donor–acceptor (EDA) complexes, whose absorption spectra display a bathochromic shift relative to their constituent parts, thus enabling photoexcitation with visible-light.[6]

These strategies have enabled the development of a broad range of radical transformations that proceed via visible-light-mediated PET under catalyst-free conditions. However, such reactions are typically limited to the generation of perfluoroalkyl or stabilized alkyl radicals.[5,7,8] Access to non-stabilized alkyl radicals under such conditions is considerably more challenging,[9,10] with only a single report by Melchiorre and co-workers that generates secondary alkyl radicals via direct photoexcitation of 4-alkyl-1,4-dihydropyridine derivatives.[11] We sought an alternative functional group that could act as a versatile photoactive handle for catalyst-free generation of non-stabilized carbon-centered radicals. One possibility was Katritzky *N*-alkylpyridinium salts **1**, which are easily prepared from primary amines **2** by reaction with 2,4,6-triphenylpyrylium **3**, are air and moisture stable, and allow selective deaminative transformations of abundant amino groups (Scheme 1A).[12] While these redox active amines have recently been applied to a number of radical-mediated transformations, they usually rely on catalysis to promote single-electron transfer (SET)-induced deamination.[13,14]

We recently reported a catalyst-free deaminative borylation reaction that proceeds via EDA complex formation between **1** and bis(catecholato)diboron (B_2cat_2) (Scheme 1B).[15] Subsequent PET and fragmentation provided efficient access to non-stabilized alkyl radicals that were intercepted by the diboron reagent. We reasoned that the 2,4,6-triphenylpyridinium moiety in **1** could be complexed with other electron-donors to generate EDA complex **4**,[16] thus providing a photoactive handle capable of generating non-stabilized alkyl radicals for application in a diverse range of C–C or C–X bond forming reactions (Scheme 1B). Herein, we report that Katritzky pyridinium salts are versatile substrates for photoinduced deaminative functionalizations of primary amines under catalyst-free conditions.



Scheme 1. Radical-mediated transformations of Katritzky pyridinium salts.

[a] Dr. J. Wu, Mr. P. S. Grant, Dr. X. Li, Dr. A. Noble, Prof. Dr. V. K. Aggarwal
School of Chemistry, University of Bristol
Cantock's Close, Bristol, BS8 1TS (UK)
E-mail: v.aggarwal@bristol.ac.uk

[†] These authors contributed equally to this work.

Supporting information for this article is given via a link at the end of the document.

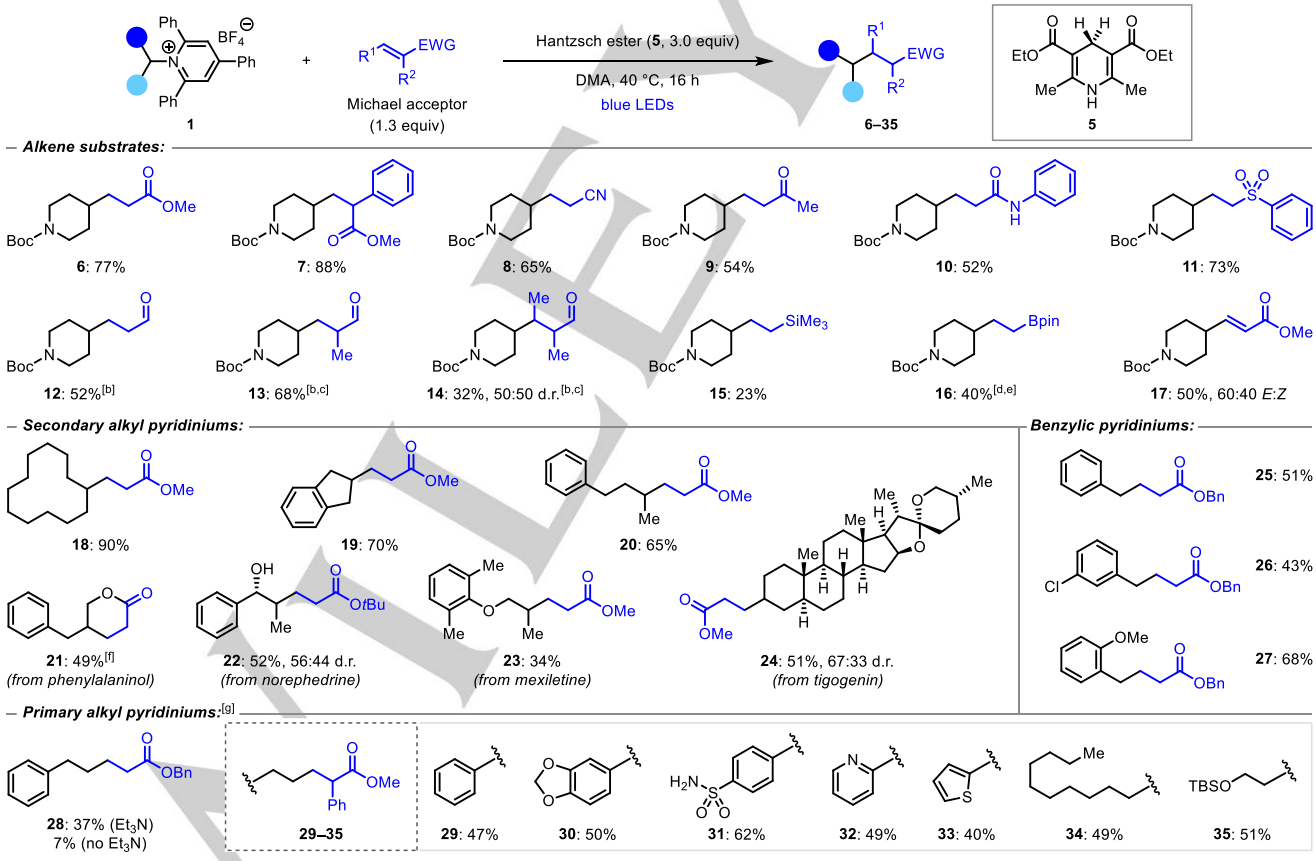
Our investigations began by studying the use of pyridiniums **1** in Giese reactions with electron-deficient alkenes (Table 1). Such reactions are well-developed using photocatalysis, but there are few reports of photoinduced reactions under catalyst-free conditions.[17] Given the overall transformation is reductive, a stoichiometric reductant was required. We selected Hantzsch ester (**5**) as this would act as a reductant but could also function as an electron-donor to form the key EDA complex with **1**.[10c,d] Gratifyingly, irradiation (λ_{max} = 450 nm) of a mixture of 4-aminopiperidine-derived pyridinium **1a**, Hantzsch ester, and methyl acrylate in DMA yielded the desired Giese adduct **6** in 77% yield (Table 1). Control experiments confirmed the necessity of light and **5** for successful reaction, and alternative reductants, such as Et_3N, gave no desired product.[18]

These optimized conditions were subsequently applied to a broad range of Michael acceptors (Table 1). Giese products from reactions with substituted acrylates (**7**), acrylonitrile (**8**), methyl vinyl ketone (**9**), *N*-phenylacrylamide (**10**), and phenyl vinyl sulfone (**11**) were formed in good to excellent yields. Aldehydes were tolerated (**12**–**14**), although the substituted enals methacrolein (**13**) and tiglic aldehyde (**14**) required higher temperatures for successful reaction. Interestingly, vinyl silanes and boronic esters were also suitable substrates, providing products **15** and **16**, respectively, albeit in low yield. Finally, methyl propiolate underwent the Giese reaction to give alkene product **17** as a mixture of *E* and *Z* isomers.

With respect to the pyridinium salts, a variety of cyclic (**18** and **19**) and acyclic (**20**) secondary alkyl substrates reacted efficiently. The Giese product from a γ-amino alcohol-derived pyridinium could be cyclized by treatment with acid to generate lactone **21**. Alternatively, *t*-butyl acrylate could be used in place of methyl acrylate to inhibit lactonization, allowing isolation of norephedrine-derived alcohol **22**. Pharmaceutical and natural product derivatives were also readily accessed, as exemplified by the formation of product **23**, from the anti-arrhythmic drug mexiletine, and **24**, from the steroid tigogenin.

While primary benzylic pyridiniums yielded products **25**–**27** in good yields, primary non-benzylic substrates failed to undergo the deaminative Giese reaction. However, we found that adding Et_3N to the reaction mixture and increasing the reaction temperature to 60 °C had a dramatic effect on the outcome of the reaction and enabled the isolation of adduct **28**, albeit in low yield. Switching from benzyl acrylate to the more activated alkene

Table 1. Giese reaction substrate scope.[a]



[a] General conditions: Pyridinium (0.2 mmol, 1.0 equiv), Michael acceptor (1.3 equiv) and **5** (3.0 equiv) in DMA (0.5 M) at 40 °C for 16 h. Yields are of isolated products after flash column chromatography. [b] Isolated as the alcohol after reduction with $NaBH_4$. [c] Reaction performed at 60 °C for 40 h. [d] Isolated as the alcohol after oxidation with $NaBO_3$. [e] Using 1.8 equiv of vinylboronic acid pinacol ester. [f] Lactonization was promoted by treatment with Amberlyst®. [g] Reactions performed at 60 °C in DMA (0.25 M) with the addition of Et_3N (3.0 equiv). DMA = *N*,*N*-dimethylacetamide. TBS = *tert*-butyldimethylsilyl.

methyl 2-phenylacrylate provided further improvements and enabled isolation of product **29** in 47% yield. Despite the yield being moderate, this result is notable as it is a rare example of a photoinduced Giese reaction of a non-stabilized primary alkyl radical under mild and catalyst-free conditions. With these new conditions, a range of non-benzylic primary alkyl pyridiniums reacted to give the Giese products (**29**–**35**) in moderate to good yields. Furthermore, the functional group tolerance of the methodology was highlighted by generating products bearing primary sulphonamide (**31**), pyridine (**32**), thiophene (**33**), and silyl ether (**35**) moieties.

To shed light on the mechanism of this catalyst-free Giese reaction, we analyzed the reaction components by UV/Vis absorption spectroscopy. DMA solutions of secondary alkyl pyridinium **36** and Hantzsch ester (**5**) were both found to absorb in the visible region (>400 nm) (Figure 1A). However, a mixture of **36** and **5** displayed a significant red-shift in absorbance, confirming formation of the postulated EDA complex. A similar shift was observed with a mixture of primary alkyl pyridinium **37** and **5** (Figure 1B). Interestingly, a mixture of **37**, **5** and Et_3N showed a further bathochromic shift, suggesting the formation of a ternary EDA complex, which could contribute to the enhanced reactivity observed with primary alkyl pyridiniums upon addition of Et_3N. The formation of alkyl radical intermediates was confirmed by a radical clock experiment with cyclopropylmethyl pyridinium **38**, during which ring-opening occurred to give alkene **39** as the only observable product (Figure 1C).

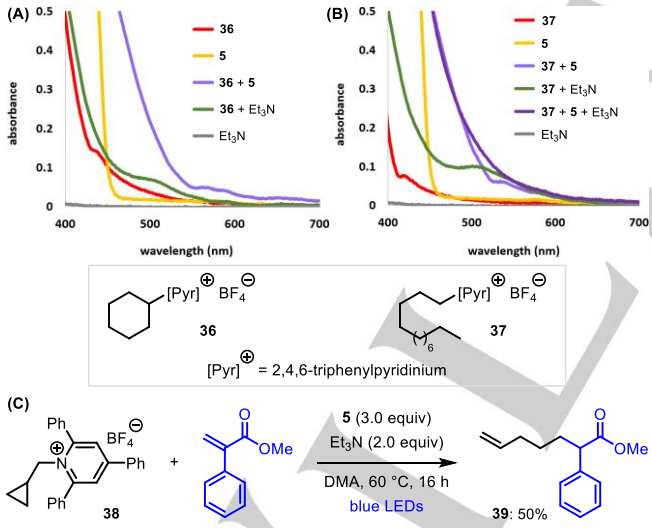


Figure 1. Mechanistic studies. (A) Spectrophotometry of pyridinium **36**. (B) Spectrophotometry of pyridinium **37**. (C) Radical clock experiment.

These results suggest a mechanism comprised of initial formation of an EDA complex **40** between the electron-deficient pyridinium **1** and electron-rich Hantzsch ester (**5**) (Figure 2). Subsequent PET leads to dihydropyridine radical cation **41** and radical **42**, the latter of which fragments to triphenylpyridine **43** and alkyl radical **44**. Addition of **44** to methyl acrylate generates radical **45**, which undergoes hydrogen atom transfer (HAT) with dihydropyridine radical cation **41** (BDFE = 31 kcal mol^{-1})[19] or **5** (BDFE = 69 kcal mol^{-1})[19] to form Giese product **46** (BDFE ≈ 96 kcal mol^{-1})[20] and pyridinium **47** or dihydropyridine radical **48**, respectively.[21]

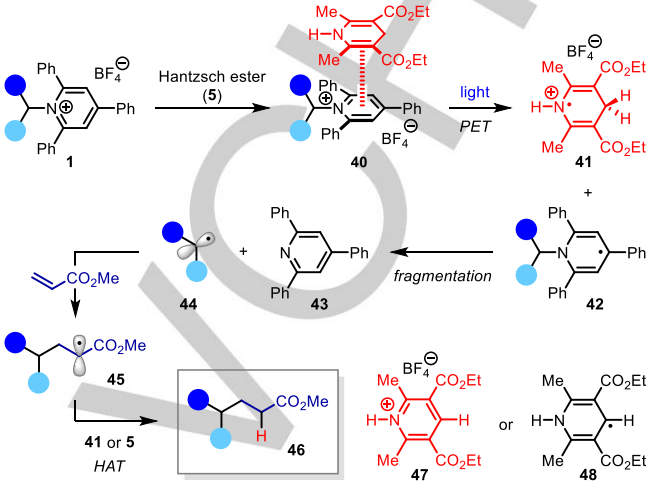
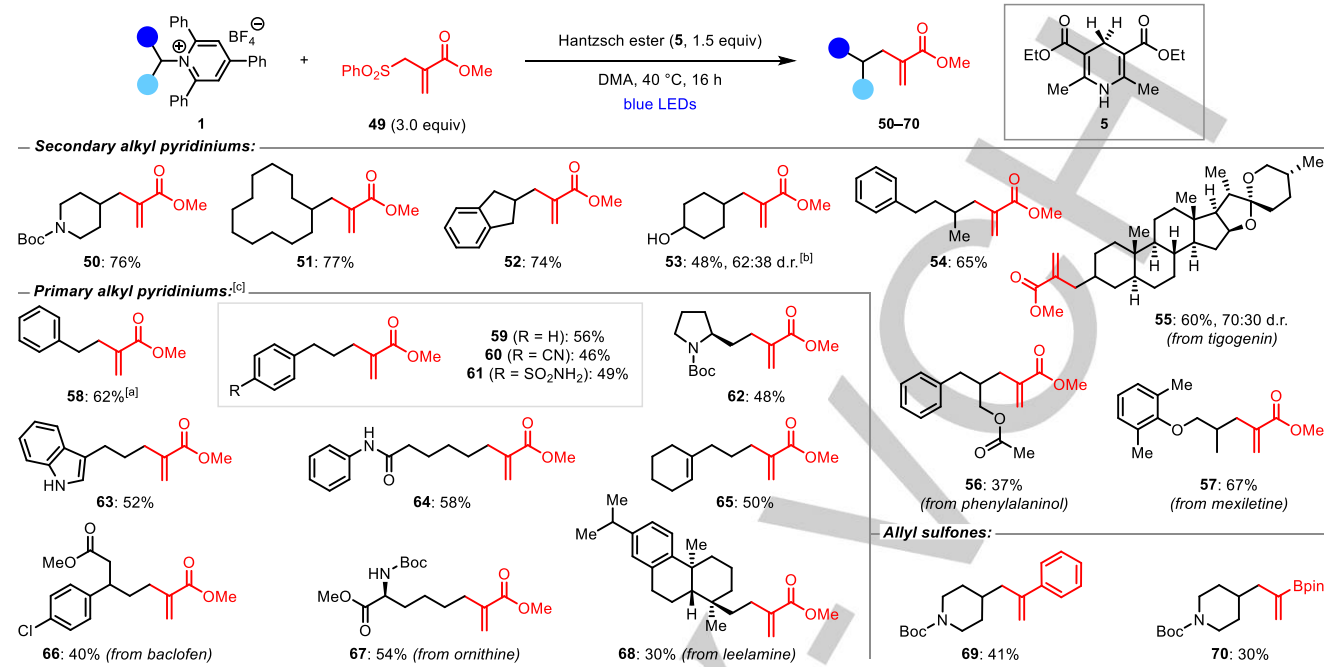


Figure 2. Proposed mechanism.

Encouraged by the results of the Giese reaction, we proceeded to investigate other catalyst-free transformations. Pleasingly, with only slight modification to the reaction conditions,[18] allylation reactions with allyl sulfone **49** were also found to be efficient (Table 2).[14c] A range of secondary alkyl pyridiniums underwent the catalyst-free deaminative allylation to give products **50**–**57** in moderate to good yields. As with the Giese reaction, although benzylic pyridiniums yielded the allylation product (**58**) under these conditions, primary alkyl pyridiniums (**59**–**68**) required the addition of Et_3N for successful reaction. The allylation reaction was found to tolerate a diverse range of functional groups, including alcohols (**53**), nitriles (**60**), sulphonamides (**61**), unprotected indoles (**63**), olefins (**65**), and secondary carbamates (**67**), and was also applied to various pharmaceuticals (**57** and **66**) and natural product derivatives (**55**, **56**, **67** and **68**). Furthermore, the use of other allyl sulfone reagents enabled the preparation of styrene derivative **69** and alkenylboronic ester **70**.

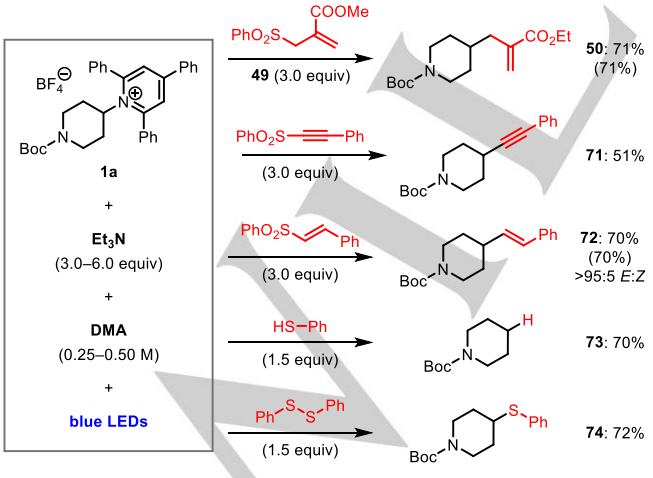
During our UV/Vis absorbance studies of pyridinium **36** we found that it also forms an EDA complex with Et_3N (Figure 1A). Thus, we were curious as to whether these photoinduced reactions could be performed with Et_3N in place of Hantzsch ester. While the Giese reaction proceeded with low yield, the allylation reaction proceeded smoothly to generate **50** in 71% when using 6.0 equiv of Et_3N in place of Hantzsch ester (Scheme 2).[18] An identical result was also obtained when Et_3N was replaced by iPr_2NEt. This result is intriguing given that these conditions are very similar to the photoredox-catalyzed conditions recently reported by Liu and co-workers, which differ only by the use of an iridium photocatalyst.[14c] We also investigated other addition–elimination reactions with unsaturated sulfone reagents and found that alkynylation and vinylation reactions also proceeded under our catalyst-free conditions, generating alkyne **71** and alkene **72**

Table 2. Allylation reaction substrate scope.[a]



[a] General conditions: Pyridinium (1.0 equiv), allyl sulfone (3.0 equiv) and **5** (1.5 equiv) in DMA (0.4 M) at 40 °C for 16 h. Yields are of isolated products after flash column chromatography. [b] Isolated after acetyl protection of the alcohol. [c] Reactions performed at 60 °C with **5** (2.5 equiv) and Et_3N (3.0 equiv).

in good yields. Again, these conditions are similar to previously reported photoredox-catalyzed protocols by Gryko and co-workers but proceed efficiently in the absence of a photocatalyst.[14b] Finally, we found that by replacing the unsaturated sulfones with other sulfur-based reagents, under otherwise identical conditions, high yielding hydrodeamination and deaminative thioetherification reactions were also possible, providing good yields of *N*-Boc-piperidine **73** and thioether **74**, respectively.



Scheme 2. Deaminative transformations promoted by Et_3N. Yields in parentheses are for reactions performed using iPr_2NEt in place of Et_3N.

In conclusion, we have described the development of a general catalyst-free deaminative protocol for the generation of non-stabilized alkyl radicals, proceeding via visible-light photoexcitation of EDA complexes of *N*-alkylpyridinium salts. The radicals were shown to undergo a range of transformations, including Giese, allylation, vinylation, alkynylation, HAT, and thioetherification reactions. The mild conditions, high functional group tolerance and ease of synthesis of the pyridinium substrates make this a useful catalyst-free approach to alkyl radical formation.

Acknowledgements

We thank EPSRC (EP/I038071/1) and H2020 ERC (670668) for financial support. P.S.G thanks the University of Auckland for a Doctoral Scholarship. X.L thanks the Fundamental Research Funds for the Central Universities (grant number GK201603034). We thank Dr. Lin He for helping with the synthesis of pyridinium salt starting materials.

Keywords: Deamination • Photochemistry • Radical Reactions • Electron Donor–Acceptor Complexes • Giese Reactions

[1] a) S. Protti, M. Fagnoni, *Photochem. Photobiol. Sci.* **2009**, *8*, 1499; b) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527; c) L. Buzzetti, G. E. M. Crisenza, P. Melchiorre, *Angew. Chem. Int. Ed.* **2018**, DOI: 10.1002/anie.201809984.

[2] a) *Visible Light Photocatalysis in Organic Chemistry* (Eds.: C. R. J. Stephenson, T. P. Yoon, D. W. C. MacMillan), Wiley-VCH, Weinheim,

2018; b) J. W. Tucker, C. R. J. Stephenson, *J. Org. Chem.* **2012**, *77*, 1617; c) M. H. Shaw, J. Twilton, D. W. C. MacMillan, *J. Org. Chem.* **2016**, *81*, 6898; d) K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev.* **2016**, *116*, 10035; e) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075.

[3] a) N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052; b) T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* **2011**, *50*, 1000; *Angew. Chem.* **2011**, *123*, 1032.

[4] M. Silvi, P. Melchiorre, *Nature* **2018**, *554*, 41.

[5] For selected examples, see: a) G. Cecere, C. M. König, J. L. Alleva, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2013**, *135*, 11521; b) M. Silvi, E. Arceo, I. D. Jurberg, C. Cassani, P. Melchiorre, *J. Am. Chem. Soc.* **2015**, *137*, 6120; c) M. Silvi, C. Sandford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2017**, *139*, 5736; d) A. Bahamonde, P. Melchiorre, *J. Am. Chem. Soc.* **2016**, *138*, 8019; e) G. Filippini, M. Silvi, , P. Melchiorre, *Angew. Chem. Int. Ed.* **2017**, *56*, 4447; *Angew. Chem.* **2017**, *129*, 4518; f) M. Silvi, C. Verrier, Y. P. Rey, L. Buzzetti, P. Melchiorre, *Nat. Chem.* **2017**, *9*, 868; g) P. Bonilla, Y. P. Rey, C. M. Holden, P. Melchiorre, *Angew. Chem. Int. Ed.* **2018**, *57*, 12819; *Angew. Chem.* **2018**, *130*, 13001; h) G. Goti, B. Bieszczad, A. Vega-Peñaloza, P. Melchiorre, *Angew Chem. Int. Ed.* **2019**, *58*, 1213; *Angew. Chem.* **2019**, *131*, 1226.

[6] a) S. V. Rosokha, J. K. Kochi, *Acc. Chem. Res.* **2008**, *41*, 641; b) C. G. S. Lima, T. de M. Lima, M. Duarte, I. D. Jurberg, M. W. Paixão, *ACS Catal.* **2016**, *6*, 1389; c) A. Postigo, *Eur J. Org. Chem.* **2018**, *2018*, 6391.

[7] For selected examples of perfluoroalkyl radical generation, see: a) P. V. Pham, D. A. Nagib, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2011**, *50*, 6119; *Angew. Chem.* **2011**, *123*, 6243; b) M. Nappi, G. Bergonzini, P. Melchiorre, *Angew. Chem. Int. Ed.* **2014**, *53*, 4921; *Angew. Chem.* **2014**, *126*, 5021; c) Ł. Woźniak, J. J. Murphy, P. Melchiorre, *J. Am. Chem. Soc.* **2015**, *137*, 5678; d) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. J. Stephenson, *Chem* **2016**, *1*, 456; e) M. L. Spell, K. Deveaux, C. G. Bresnahan, B. L. Bernard, W. Sheffield, R. Kumar, J. R. Ragains, *Angew. Chem. Int. Ed.* **2016**, *55*, 6515; *Angew. Chem.* **2016**, *128*, 6625; f) Y. Cheng, S. Yu, *Org. Lett.* **2016**, *18*, 2962; g) Y.-Y. Liu, X.-Y. Yu, J.-R. Chen, M.-M. Qiao, X. Qi, D.-Q. Shi, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2017**, *56*, 9527; *Angew. Chem.* **2017**, *129*, 9655; h) H.-Y. Tu, S. Zhu, F.-L. Qing, L. Chu, *Chem. Commun.* **2018**, *54*, 12710; i) Q. Guo, M. Wang, H. Liu, R. Wang, Z. Xu, *Angew. Chem. Int. Ed.* **2018**, *57*, 4747; *Angew. Chem.* **2018**, *130*, 4837.

[8] For stabilized alkyl radical generation, see: a) E. Arceo, I. D. Jurberg, A. Álvarez-Fernández, P. Melchiorro, *Nat. Chem.* **2013**, *5*, 750; b) E. Arceo, A. Bahamonde, G. Bergonzini, P. Melchiorro, *Chem. Sci.* **2014**, *5*, 2438; c) S. R. Kandukuri, A. Bahamonde, I. Chatterjee, I. D. Jurberg, E. C. Escudero-Adán, P. Melchiorre *Angew. Chem. Int. Ed.* **2015**, *54*, 1485; *Angew. Chem.* **2015**, *127*, 1505; d) Z.-Y. Cao, T. Ghosh, P. Melchiorre, *Nat. Commun.* **2018**, *9*, 3274; e) C.-W. Hsu, H. Sundén, *Org. Lett.* **2018**, *20*, 2051.

[9] For aryl radical generation, see: a) M. A. Fox, J. Younathan, G. E. Fryxell, *J. Org. Chem.* **1983**, *48*, 3109; b) M. Tobisu, T. Furukawa, N. Chatani, *Chem. Lett.* **2013**, *42*, 1203; c) L. Marzo, S. Wang, B. König, *Org. Lett.* **2017**, *19*, 5976; d) B. Liu, C.-H. Lim, G. M. Miyake, *J. Am. Chem. Soc.* **2017**, *139*, 13616.

[10] For heteroatom-centered radical generation, see: a) J. Davies, S. G. Booth, S. Essafi, R. A. W. Dryfe, D. Leonori, *Angew. Chem. Int. Ed.* **2015**, *54*, 14017; *Angew. Chem.* **2015**, *127*, 14223; b) D. F. Reina, E. M. Dauncey, S. P. Morcillo, T. D. Svejstrup, M. V. Popescu, J. J. Douglas, N. S. Sheikh, D. Leonori, *Eur. J. Org. Chem.* **2016**, *2017*, 2108; c) J. Zhang, Y. Li, R. Xu, Y. Chen, *Angew. Chem. Int. Ed.* **2017**, *56*, 12619; *Angew. Chem.* **2017**, *129*, 12793; d) Y. Li, J. Zhang, D. Li, Y. Chen, *Org. Lett.* **2018**, *20*, 3296.

[11] L. Buzzetti, A. Prieto, S. R. Roy, P. Melchiorre, *Angew Chem. Int. Ed.* **2017**, *56*, 15039; *Angew Chem.* **2017**, *129*, 15235.

[12] J. B. Bapat, R. J. Blade, A. J. Boulton, J. Epsztajn, A. R. Katritzky, J. Lewis, P. Molina-Buendia, P.-L. Nie, C. A. Ramsden, *Tetrahedron Lett.* **1976**, *17*, 2691.

[13] For nickel-catalyzed reactions, see: a) C. H. Basch, J. Liao, J. Xu, J. J. Piane, M. P. Watson, *J. Am. Chem. Soc.* **2017**, *139*, 5313; b) J. Liao, W. Guan, B. P. Boscoe, J. W. Tucker, J. W. Tomlin, M. R. Garnsey, M. P. Watson, *Org. Lett.* **2018**, *20*, 3030; c) W. Guan, J. Liao, M. P. Watson, *Synthesis* **2018**, *50*, 3231.

[14] For photoredox-catalyzed reactions, see: a) F. J. R. Klauck, M. J. James, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 12336; *Angew. Chem.* **2017**, *129*, 12505; b) M. Ociepa, J. Turkowska, D. Gryko, *ACS Catal.* **2018**, *8*, 11362; c) M.-M. Zhang, F. Liu, *Org. Chem. Front.* **2018**, *5*, 3443; d) F. J. R. Klauck, H. Yoon, M. J. James, M. Lautens, F. Glorius, *ACS Catal.* **2019**, *9*, 236.

[15] a) J. Wu, L. He, A. Noble, V. K. Aggarwal, *J. Am. Chem. Soc.* **2018**, *140*, 10700; b) J. Hu, G. Wang, S. Li, Z. Shi, *Angew. Chem. Int. Ed.* **2018**, *57*, 15227; *Angew. Chem.* **2018**, *130*, 15447; c) F. Sandfort, F. Strieth-Kalthoff, F. J. R. Klauck, M. J. James, F. Glorius, *Chem. Eur. J.* **2018**, *24*, 17210; For a mecahistically related decarboxylative borylation, see: d) A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* **2017**, *357*, 283.

[16] For EDA complexes of Katritzky pyridiniums, see: a) A. R. Katritzky, G. Z. de Ville, R. C. Patel, *Tetrahedron Lett.* **1980**, *21*, 1723; b) A. R. Katritzky, G. De Ville, R. C. Patel, *Tetrahedron* **1981**, *37*, 25.

[17] a) K. Okada, K. Okamoto, N. Morita, K. Okubo, M. Oda, *J. Am. Chem. Soc.* **1991**, *113*, 9401; b) G. L. Lackner, K. W. Quasdorf, G. Pratsch, L. E. Overman, *J. Org. Chem.* **2015**, *80*, 6012; c) G. Pratsch, G. L. Lackner, L. E. Overman, *J. Org. Chem.* **2015**, *80*, 6025.

[18] See Supporting Information for details.

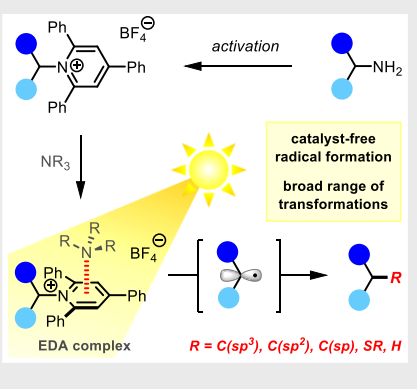
[19] X.-Q. Zhu, H.-R. Li, Q. Li, T. Ai, J.-Y. Lu, Y. Yang, J.-P. Cheng, *Chem. Eur. J.* **2003**, *9*, 871.

[20] J. J. Brocks, H.-D. Beckhaus, A. L. J. Beckwith, C. Rüchardt, *J. Org. Chem.* **1998**, *63*, 1935.

[21] See Supporting Information for further mechanistic discussions and evidence for the formation of radicals **42** and **48**.

COMMUNICATION

Electron donor–acceptor complexes between pyridinium-activated primary amines and Hantzsch ester or triethylamine undergo catalyst-free photoinduced single-electron transfer with visible-light. Fragmentation leads to alkyl radicals that could be intercepted with a variety of acceptors. This deaminative radical generation was applied to catalyst-free Giese, allylation, vinylation, alkynylation, thioetherification, and hydrodeamination reactions.



*Jingjing Wu, Phillip S. Grant, Xiabing Li, Adam Noble, Varinder K. Aggarwal**

Page No. – Page No.

Catalyst-Free Deaminative Functionalizations of Primary Amines via Photoinduced Single-Electron Transfer